

PCT/EP2004/00010



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference NAB878_03PCT	FOR FURTHER ACTION	See Form PCT/TPA/416
International application No. PCT/EP2004/000100	International filing date (day/month/year) 09 January 2004 (09.01.2004)	Priority date (day/month/year) 09 January 2003 (09.01.2003)
International Patent Classification (IPC) or national classification and IPC C12N 1/15		
Applicant BASF AKTIENGESELLSCHAFT		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>7</u> sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising: a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows: <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items: <input checked="" type="checkbox"/> Box No. I Basis of the report <input type="checkbox"/> Box No. II Priority <input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input checked="" type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application

Date of submission of the demand 15 July 2004 (15.07.2004)	Date of completion of this report 31 January 2005 (31.01.2005)
Name and mailing address of the IP/EA/EP Facsimile No.	Authorized officer Telephone No.

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International application No.

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Box No. 1 Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):

- ☐ The international application as originally filed/furnished
- ☒ the description:
- pages _____ 1-62 _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ the claims:
- pages _____ 1-38 _____, as originally filed/furnished
- pages* _____, as amended (together with any statement) under Article 19
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ the drawings:
- pages _____ 1/24-24/24 _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (specify): _____
- ☐ any table(s) related to sequence listing (specify): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (specify): _____
- ☐ any table(s) related to sequence listing (specify): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. 1, Item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis that of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purpose of search and/or examination
 - ☐ received by this Authority as an amendment* on _____
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

* If item 4 in Box No. 1 applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded".

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	2, 8, 10-13, 15-18, 21, 24-30, 34, 36-38	YES
	Claims	1, 3-7, 9, 14, 19, 20, 22, 23, 31-33, 35	NO
Inventive step (IS)	Claims		YES
	Claims	1-38	NO
Industrial applicability (IA)	Claims	1-38	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Reference is made to the following documents:

- D1: WO 98/46772 A
- D2: VAN HEESWIJCK ET AL. (1984) CARLSBERG RES. COMM. 49, 691-702
- D3: NAVARRO ET AL. (2000) EUR. J. BIOCHEM. 267, 800-807
- D4: NAVARRO ET AL (2001) MOL. GENET. GENOMICS. 266, 463-470
- D5: SKORY (2002) MOL GENET. GENOMICS. 268, 397-406
- D6: US-B1-6 413 736
- D7: US 2002/051998 A1
- D8: LEE ET AL (2002) APP. MICROBIOL. BIOTECHNOL. 60, 1-11
- D9: AN ET AL. (1996) GENE 176, 93-96
- D10: NICOLAS ET AL. (2003) EMBO J. 22, 3983-3991

D10 is not considered prior art pursuant to PCT Rule 64.1.

Novelty (PCT Article 33(2))

The present application does not meet the requirements of

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Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, objections and explanations supporting such statement

PCT Article 33(1) because the subject matter of claims 1, 3 to 7, 9, 14, 19, 20, 22, 23, 31 to 33 and 35 lacks novelty (PCT Article 33(2)).

Document D1 is considered the prior art closest to the subject matter of claim 1 and discloses the production of genetically transformed filamentous fungi and fungi of the *Blakeslea* genus (page 16, line 6). The intention is to use the produced fungi for producing secondary metabolites and carotenoids (page 27, line 9). It is also the intention to carry out genetic engineering of the genome, for example by homologous recombination. D1 discloses (page 19, lines 5 to 29) that if the genetically engineered fungi are intended for the production of secondary metabolites, then expression cassettes with the requisite genes can be introduced into the genome. The selection and propagation of the genetically engineered cells are disclosed, for example, in claim 21. A method for producing metabolites is disclosed in claim 28.

D1 is considered prejudicial to novelty, since the examiner is of the opinion that the information in D1 matches the imprecise and broad wording of the present claims.

Inventive step (PCT Article 33(3))

The present application does not meet the requirements of PCT Article 33(1) because the subject matter of claims 1 to 38 does not involve an inventive step (PCT Article 33(3)).

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Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

The subject matter of claim 2 differs from that known from D1 in that the method is restricted to fungi of the *Blakeslea trispora* type.

The present invention can thus be considered to address the problem of developing a method for producing genetically engineered *Blakeslea trispora*.

In view of the fact that

- claim 1 does not contain any special features relating to the transformation,
- D1 discloses the production of genetically engineered fungi of the *Blakeslea* genus,
- organisms of the *Blakeslea trispora* type are known for their production of B-carotene, and
- genetic mutations for increasing carotenoid production of the *Blakeslea trispora* type are known,

an inventive step cannot be acknowledged in respect of claim 2.

The use of a plasmid containing a *gpdA* promoter, *hph* resistance gene and/or *trpC* terminator for transformation purposes is also not inventive, since it is already known from D9 (see figure 1).

As has already been mentioned in the description of the present application, homokaryotisation is necessary only when a genomic gene deletion is intended to be carried out, not, however, when genes are intended to be added, and was disclosed in D1, D2, D3, D4 and D5. As an alternative to homokaryotisation, it would also be

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<p>possible, however, to carry out RNA silencing (see D3 and D4).</p> <p>D6, D7 and D8 disclose the genetic production of carotenoids and xanthophylls, and transformed organisms which contain the genes required therefor. It is obvious to use this knowledge to genetically produce organisms of the <i>Blakeslea</i> genus, since it is known that said organisms produce large quantities of B-carotene.</p> <p>The vector with SEQ ID NO:3 is derived from the known vector pANsCOS1, which was developed for the transformation of fungi (Osiewacz (1994) Curr. Genet. 26, 87-90). The use of the vector with SEQ ID NO:3 and the vectors derived therefrom in a method for the transformation of <i>Blakeslea</i> is therefore non-inventive.</p>		

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Box No. VI Certain documents cited			
1. Certain published documents (Rule 70.10)			
Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
2. Non-written disclosures (Rule 70.9)			
Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)	
See Supplemental Sheet			

Form PCT/PEA/409 (Box No. VI) (April 2005)